

REMARKS

Claims 3 and 16 stand amended to correct typographical errors.

New claims 25-27 are amended versions of claims 19-21, wherein a specific subset of residues has been selected. Support for the new claims is found, for example, page 28, lines 6-13, and elsewhere in the claims and specification as originally filed.

No new matter is added by way of the amendments to the claims or by way of the new claims.

Applicants note that the subject matter of the new claims is believed to be novel over the cited references, and is nowhere suggested by the combination of the cited references.

Applicants acknowledge the withdrawal of previous rejections as noted by the USPTO on page 2 of the instant Office Action.

Claims 1, 3, 6-8, 10-12, 14, 16, and 19-24 are pending in the application, and stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. 6,017,886 to Carnahan (hereafter "Carnahan") in view of U.S. Patent 5,367,060 to Vandlen *et al.* ("Vandlen").

Applicants respectfully traverse the claim rejections.

The Rejections of Claims 1, 3, 6-8, 10-12, 14, 16, and 19-24 under 35 U.S.C. §103(a)

Claims 1, 3, 6-8, 10-12, 14, 16, and 19-24 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent 6,017,886 to Carnahan ("Carnahan") in view of U.S. Patent 5,367,060 (hereafter "'060").

In order to establish a prima facie case of obviousness, there must be 1) some suggestion or motivation in the art or in the knowledge generally available to one of ordinary skill in the art, to modify or to combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed

combination and the reasonable expectation of success must be found in the prior art, and not based on the applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The USPTO cites Carnahan in view of Vandlen as allegedly making the present invention obvious. The USPTO suggests that "Carnahan teaches that heregulin- β 1 is one of many heregulin peptides that are effective in stimulating utricular sensory epithelial cells" (page 2 of the instant Office Action).

However, Applicants note that the present claims are directed to methods utilizing heregulin **fragments and variants** thereof that meet explicit and restrictive criteria recited in the claims. The reference to heregulin- β 1, for example, is not believed to refer to a heregulin **fragment or variant** and is not believed to provide any suggestion or motivation to use a heregulin fragment or variant, much less the specific heregulin fragments and variants of the present invention.

Moreover, no combination of references suggests that fragments of a **single heregulin molecule, or variants thereof**, could be effective in the present methods.

In particular, the cited references, even if combined, lack disclosure or suggestion of the heregulin fragments and variants of the claimed invention, and so fail to provide all the elements of the claimed invention. Lacking these elements, and lacking any suggestion or motivation to provide these elements, there is no motivation to combine these references in an attempt to provide the claimed invention. Even if the cited references were to be combined in the absence of any teaching or motivation to do so, they would fail to provide the present invention with all the limitations of the pending claims. Thus, the combined references fail to provide any reasonable expectation of success for the combination. In fact, Carnahan, which uses an intact heregulin and a fusion protein including sequences from two **different** heregulins, teaches away from the present invention, which requires heregulin fragments from a single heregulin molecule instead of a combination from two different heregulins. Neither reference suggests the N-terminal or C-terminal sites of the present invention,

nor does either reference suggest the sites named as suitable for substitution, deletion, or insertion.

Accordingly, Carnahan, discussing the use of whole heregulin molecules, or hybrid fusion proteins of fragments from different heregulins, to stimulate utricular sensory epithelial cells, combined with the '060 patent together fail to provide the isolated ligands used in the methods of the present invention.

Accordingly, the cited references lacking any motivation or suggestion to be combined to provide the claimed invention, and lacking any reasonable expectation of success for such a combination, Applicants respectfully submit that the rejections of claims 1-8, 10-12, 14-17, and 19-24 under 35 U.S.C. §103(a) is overcome.

CONCLUSION

In view of the foregoing, it is respectfully submitted that all claims in the present application stand in condition for allowance. Applicant respectfully requests reconsideration and allowance of all claims, including consideration and allowance of the new claims. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** referencing Attorney's Docket No. **39766-0035 C1**.

Respectfully submitted,

Date: October 31, 2007

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